Complete Analysis of New Psychoactive Substances Using NMR

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Each year, more new psychoactive substances (NPS) are being formulated and produced under non-regulated conditions [1]. These substances can be purchased legally by consumers, which poses an unpredictable risk to health and a challenge to law enforcement and medical personnel. There can be a high degree of structural similarity between illegal entities and legal analogues, regioisomers for example, which means that the analytical data used during drug cases should be able to discern between those compounds with certainty.

This article shows how critical nuclear magnetic resonance (NMR) is for the unequivocal structural identification of illegal drugs and legal highs. The article demonstrates how DOSY experiments can be used along with computer-aided structure elucidation[2] of the various compounds that make up synthetic drugs such as China White. It also shows how the structural information obtained can be used to streamline the identification and quantification of compounds present in recreational drug substances through the use of library search and matching tools[3]. Figure 1 shows the NPS identified for the first time in the present year and the NPS identified in previous years.
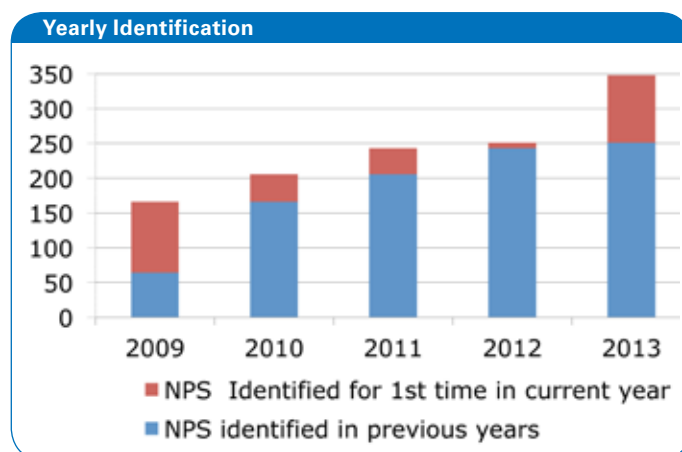

Figure 1: NPS identified from year 2009 to 2013

Ketamine - Confirming Regioisomerism

NMR was used to analyze a Ketamine sample in order to verify the structure (class B compound). Verification was achieved using CMC-se software, including long-range HC correlations. The use of the new CMC-se structure drawing tool for structure verification purposes is shown in Figure 2.
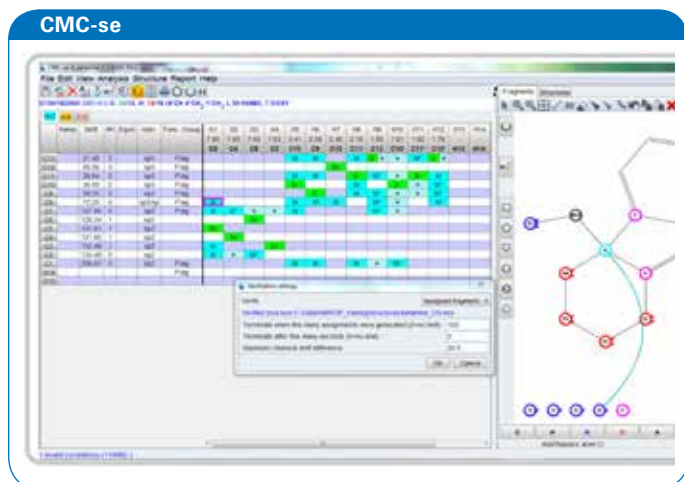

CMC-se

Figure 2: New structure builder 'white board' tool in CMC-se

China White - Mixture Analysis

Figure 3a shows the separation of compounds (A and B) that constitute China White with DOSY, and Figures 3a to 3b show the elucidation of A using CMC-se. The same methodology was carried out for compound B, which was found to be benzocaine.
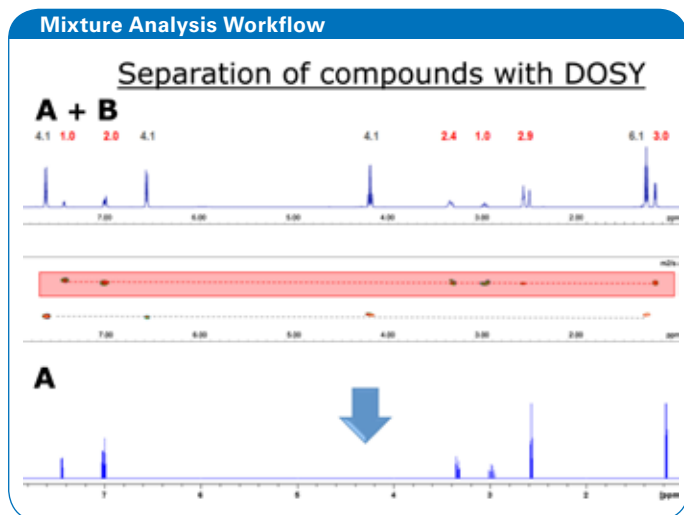

Mixture Analysis Workflow

Figure 3a: 2D DOSY spectrum illustrating the separation of compounds A and B in China White. Integral values are shown on top of the multiplets in red (A) and black (B)

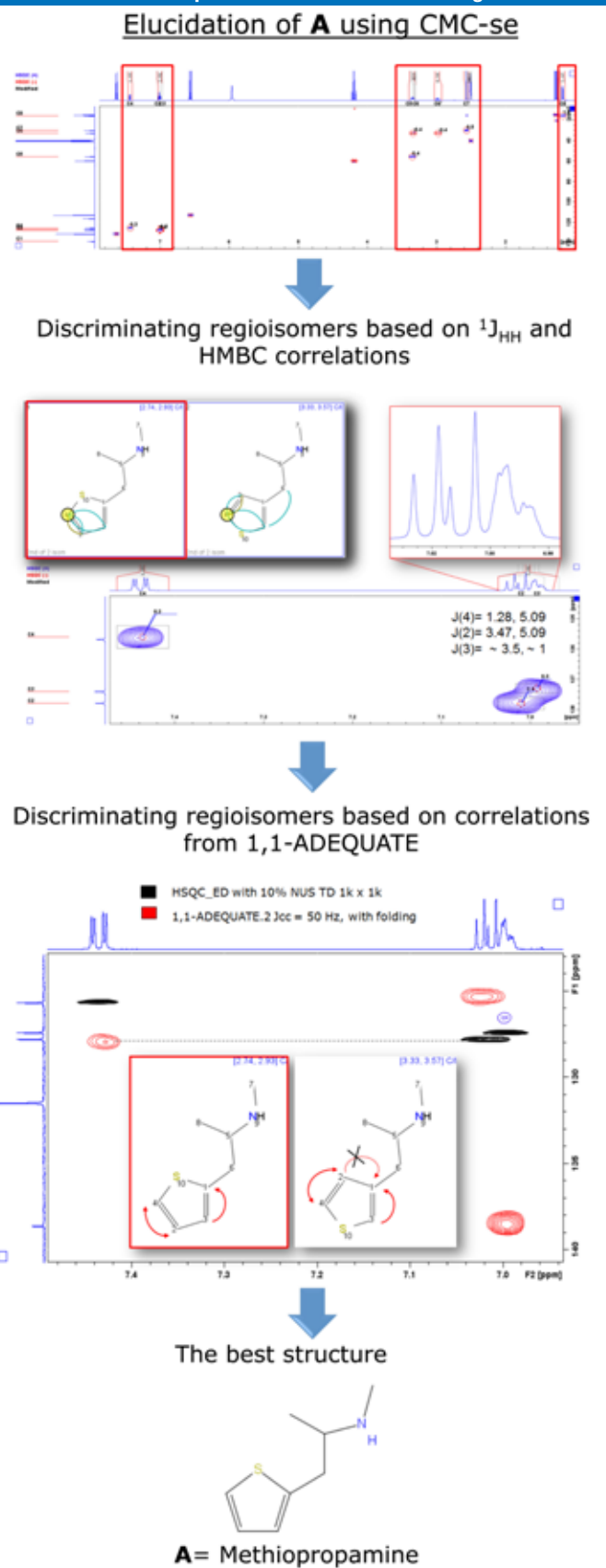**Elucidation of Compound A in China White Using CMC-se**

Figure 3b: Elucidation of A using CMC-se: selective peak picking (top) and the use of HMBC (middle) and 1,1-ADEQUATE (bottom) to discriminate regioisomers

Both the structure and the NMR spectra for benzocaine and methiopropamine were entered into a database. A method was developed for the identification and quantification of these compounds in mixtures using Assure Raw Material Screening (Assure RMS), which can be run in complete automation, from acquisition through to report creation.

By applying the newly developed Assure RMS method, further examination of other batches of China White can be carried out just with the push of a button, thereby significantly reducing the time taken for analysis.

Conclusion

NMR is a critical tool for complete analysis of NPS. NPS analysis using CMC-se software offers a number of benefits such as elucidation of NPS from scratch, differentiation of regioisomers and structure verification. It also eliminates bias and tunnel effect and allows exploration of the entire chemical space. The NPS mixture analysis workflow involved DOSY for compound separation; CMC-se of one compound at a time; and Assure RMS for compound identification, databasing and quantification.

References

1. "Global Synthetic Drugs Assessment' report, UNODC, http://www.unodc.org/documents/southeastasiaandpacific/2014/05/gsda/2014_Global_Synthetic_Drugs_Assessment_embargoed_Tokyo_web.pdf, accessed 18Dec14

2. http://www.bruker.com/products/mr/nmr/nmr-software/software/complete-molecular-confidence/cmc-se/overview.html, accessed 18Dec14

3. http://www.bruker.com/products/mr/nmr/nmr-software/software/assure/overview.html, accessed 18Dec14

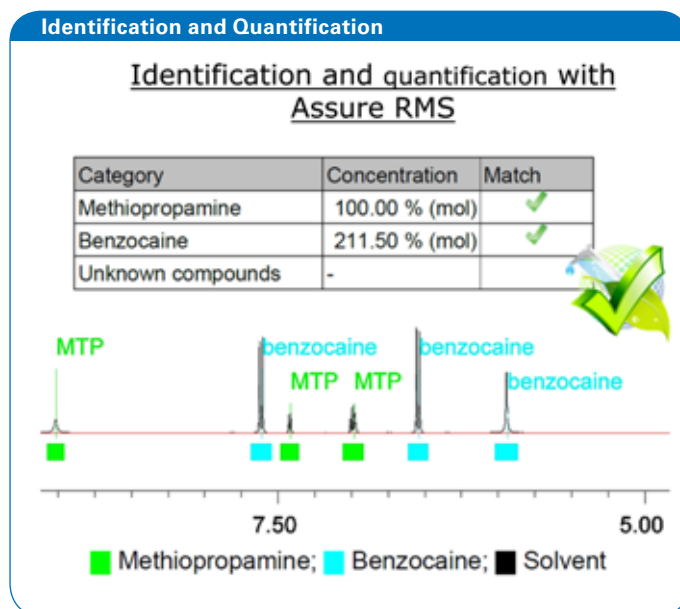**Identification and Quantification**

Figure 4: Use of Assure RMS for the rapid identification and quantification of methiopropamine and benzocaine in China White

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